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1. (Currently amended) A method for effecting an homologous recombination between a double-stranded native nucleic acid segment in a cell and a donor nucleic acid segment introduced into the cell, which method comprises the steps consisting of:

- a) introducing into a cell <u>ex vivo</u>, a nucleic acid targeting system comprising:
- (i) a third strand oligonucleotide which comprises a base sequence capable of forming a triple helix at a binding region on one or both strands of a native nucleic acid segment,
- (ii) a donor nucleic acid, comprising a nucleic acid sequence substantially homologous to the native nucleic acid segment so that the donor sequence is capable of undergoing homologous recombination with the native sequence at the target region,
- (iii) an adapter segment comprising an oligonucleotide sequence able to bind at least a portion of said donor nucleic acid through Watson-Crick base pairing, the adapter segment being linked to said third strand oligonucleotide,
- b) allowing the third strand oligonucleotide to bind to the native nucleic acid segment to form a triple helix nucleic acid, thereby inducing homologous recombination at the native nucleic acid segment target region; and
- c) allowing homologous recombination to occur between the native and donor nucleic acid segments;

wherein said donor nucleic acid is between more than 100 and 1,000,000 bases in length.

- 2. (Previously presented) The method according to claim 1, wherein said donor nucleic acid is prepared by chemical synthesis or by an amplification method.
- 3. (Original) The method according to claim 1, comprising the steps consisting of:

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a) providing a pair of primers complementary of the 5' and 3' ends of a double-stranded first native nucleic acid sequence;

- b) amplifying said first native nucleic acid sequence,
- c) isolating the amplification product thus obtained;
- d) annealing the amplification product with an adapter segment comprising an oligonucleotide sequence able to bind at least a portion of the nucleotide sequence of said amplified nucleic acid through Watson-Crick base pairing, said adapter segment being linked to a third strand oligonucleotide which comprises a base sequence capable of forming a triple helix at a binding region on one or both strands of a second native nucleic acid segment, thereby providing a nucleic acid targeting system comprising:
  - (i) said third strand oligonucleotide,
  - (ii) said amplification product as a donor nucleic acid segment, and
- (iii) said adapter segment bound to said donor nucleic acid segment through Watson-Crick base pairing;
- e) introducing said nucleic acid targeting system into a cell comprising a second native nucleic acid different from the first native nucleic acid;
- f) allowing the third strand oligonucleotide to bind to the second native nucleic acid segment to form a triple helix nucleic acid, thereby inducing homologous recombination at the second native nucleic acid segment target region; and
- g) allowing homologous recombination to occur between the second native and donor nucleic acid segments.
- 4. (Original) The method according to claim 1, wherein the donor nucleic acid is selected from the group consisting of a double-stranded nucleic acid, a substantially complementary pair of single stranded nucleic acids and a single stranded nucleic acid.
- 5. (Previously presented) The method according to claim 1, comprising the steps consisting of:

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a) providing a pair of primers complementary to the 5' and 3' ends of a first double-stranded native nucleic acid sequence, wherein one of the primers is an adapter segment linked to a third strand oligonucleotide that comprises a base sequence capable of forming a triple helix at a binding region on one or both strands of a second double-stranded native nucleic acid segment;

- b) amplifying said first native nucleic acid sequence,
- c) isolating the amplification product thus obtained, thereby providing a nucleic acid targeting system comprising:
  - (i) said third strand oligonucleotide,
  - (ii) said amplification product as a donor nucleic acid segment, and
- (iii) said adapter segment bound to a strand of said donor nucleic acid segment through Watson-Crick base pairing;
- d) introducing said nucleic acid targeting system into a cell comprising a second native nucleic acid different from the first native nucleic acid;
- e) allowing the nucleotide to bind to the second native nucleic acid segment to form a triple helix nucleic acid, thereby inducing homologous recombination at the second native nucleic acid segment target region; and
- f) allowing homologous recombination to occur between the second native and donor nucleic acid segments.
- 6. (Original) The method according to claim 1 comprising the steps consisting of:
- a) providing a pair of primers complementary to the 5' and 3' ends of a first double-stranded native nucleic acid sequence, wherein one of the primers is a modified adapter segment which contains one or several ribonucleotide(s) at its 3'-end, wherein said adapter segment is linked to a third strand oligonucleotide which comprises a base sequence capable of forming a triple helix at a binding region on one or both strands of a second double-stranded native nucleic acid segment;

- b) amplifying said first native nucleic acid sequence,
- c) isolating the amplification product thus obtained,
- d) treating the isolated amplification product in conditions sufficient to allow destruction of said ribonucleotide, thereby providing a nucleic acid targeting system comprising:
  - (i) said third strand oligonucleotide,
  - (ii) said amplification product as a donor nucleic acid segment, and
- (iii) said adapter segment bound to said donor nucleic acid segment through Watson-Crick base pairing;
- e) introducing said nucleic acid targeting system into a cell comprising a second native nucleic acid different from the first native nucleic acid;
- f) allowing the nucleotide to bind to the second native nucleic acid segment to form a triple helix nucleic acid, thereby inducing homologous recombination at the second native nucleic acid segment target region; and
- g) allowing homologous recombination to occur between the second native and donor nucleic acid segments.
- 7. (Original) The method according to claim 6, wherein step d) comprises enzymatic or mild alkaline treatment.
- 8. (Previously presented) The method according to claim 1, wherein said third strand oligonucleotide is a single DNA molecule of between 7 and 50 nucleotides.
- 9. (Previously presented) The method according to claim 1, wherein the donor nucleic acid is between more than 100 and about 3000 bases in length.
- 10. (Previously presented) The method according to claim 1, wherein the adapter is a single-stranded oligonucleotide comprising between 4 and 120 nucleotides.

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11. (Original) The method according to claim 1, wherein the adapter is linked to said third strand oligonucleotide through a spacer.

- 12. (Previously presented) The method according to claim 1, wherein the spacer comprises a hydrocarbon skeleton.
- 13. (Original) The method according to claim 11, wherein the spacer comprises a polyethyleneglycol chain or a mixed structure comprising polyethyleneglycol units and (oligo) nucleotide units.
- 14. (Previously presented) The method according to claim 11, wherein the spacer is a hexaethyleneglycol chain.
- 15. (Original) The method according to claim 1, wherein the native nucleic acid contains a mutation that is corrected by the homologous recombination.
- 16. (Original) The method according to claim 15, wherein the mutation is selected from the group consisting of base changes, deletions, insertions, nucleotide repeats, and combinations thereof.
- 17. (Original) The method according to claim 1, wherein the homologous recombination causes an alteration in the native nucleic acid sequence.
- 18. (Original) The method according to claim 17, wherein the alteration is caused in a segment selected from the group consisting of a gene, a part of a gene, a gene control region, an intron, a splice junction, a transposable element, a site specific recombination sequence, and combinations thereof.
- 19. (Original) The method according to claim 1, wherein the native nucleic acid is chromosomal.
- 20. (Original) The method according to claim 1, wherein the native nucleic acid is extrachromosomal.

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21. (Original) The method according to claim 15, wherein the native nucleic acid is selected from the group consisting of mitochondrial DNA, episomal DNA, a plasmid and chloroplast DNA.

## 22. (Withdrawn) A kit comprising:

- (i) a third strand oligonucleotide which comprises a base sequence capable of forming a triple helix at a binding region on one or both strands of a native nucleic acid segment;
- (ii) a donor nucleic acid, comprising a nucleic acid sequence substantially homologous to the native nucleic acid segment so that the donor sequence is capable of undergoing homologous recombination with the native sequence at the target region; and
- (iii) an adapter segment comprising an oligonucleotide sequence able to bind at least a portion of said donor nucleic acid through Watson-Crick base pairing, the adapter segment being linked to said third strand oligonucleotide.
- 23. (Currently amended) A method for effecting gene alteration or mutation repair at a specific-sequence site on a native DNA, comprising:
- a) introducing into a cell <u>ex vivo</u>, a nucleic acid targeting system comprising:
- (i) a third strand oligonucleotide which comprises a base sequence capable of forming a triple helix at a binding region on one or both strands of a native nucleic acid segment,
- (ii) a donor nucleic acid, comprising a nucleic acid sequence substantially homologous to the native nucleic acid segment such that the donor sequence is capable of undergoing homologous recombination with the native sequence at the target region,

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(iii) an adapter segment comprising an oligonucleotide sequence able to bind at least a portion of said donor nucleic acid through Watson-Crick base pairing, the adapter segment being linked to said third strand oligonucleotide,

- b) allowing the oligonucleotide to bind to the native nucleic acid segment to form a triple helix nucleic acid, thereby inducing homologous recombination at the native nucleic acid segment target region; and
- c) allowing homologous recombination to occur between the native and donor nucleic acid segments,

thereby performing that gene alteration or mutation repair.

- 24. (Previously presented) The method according to claim 1, wherein said third strand oligonucleotide is a single DNA molecule of between 10 and 30 nucleotides.
- 25. (Previously presented) The method according to claim 1, wherein the adapter is a single-strand oligonucleotide comprising between 8 and 30 nucleotides.
- 26. (Previously presented) The method according to claim 12, wherein the hydrocarbon skeleton is interrupted and/or substituted by one or more heteroatoms, or heterogroups that comprise at least one of these heteroatoms.